REMARKS

Status of application

Applicants note that this application has been pending since December 13, 1996, which is more than five years. In accordance with MPEP § 707.02, "[a]ny application that has been pending five years should be carefully studied by the supervisory patent examiner and every effort made to terminate its prosecution. In order to accomplish this result, the application is to be considered "special" by the examiner."

Status of the claims

Claims 1-24, 26-65, and 67-97 are pending in the present application. Claims 6-19, 38, 41, 44-53, 57, and 58 were previously withdrawn from consideration as drawn to a non-elected invention. Claims 25 and 66 were previously canceled. By virtue of this response, claims 21, 22, 24, 31, and 77 have been canceled, claims 1, 20, 39, 54, 56, 84, and 92 have been amended, and new claims 98-104 have been added. Accordingly, claims 1-5, 20, 23, 26-30, 32-37, 39-40, 42-43, 54-56, 59-65, 67-76, and 78-104 are currently under consideration.

The claim amendments and new claims are supported by the specification, for example, on page 27, lines 7-10, and on page 63, line 25 - page 77, line 11. The term "suitable" has been deleted from claims 54 and 56 in accordance with cosmetic amendments that were made in co-pending application no. 08/836,455 with traverse. No new matter has been added by the foregoing amendments.

With respect to all amendments and canceled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional applications.

Telephone interview

Applicants wish to thank Examiners Rawlings and Caputa for extending the courtesy of a telephone interview on May 7, 2003, and for the helpful discussion that ensued. Applicants appreciate the Examiners' helpful suggestions, which are reflected in this response. Applicants have given careful consideration to the issues raised in the outstanding Office Action and in the telephone interview and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Request for rejoinder

In response to Applicants' request for rejoinder of presently excluded method claims, the Examiner states that "Applicants' request is denied." Applicants respectfully draw the Examiner's attention to MPEP § 821.04, which states, "Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. . . . However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim *will be rejoined.*" (emphasis added) The Examiner does not have discretion to "deny" Applicants' request. Applicants respectfully reiterate their request rejoinder of method claims upon allowance of the composition claims.

Objections to the specification

The specification is objected to due to alleged improper use of the trademarks ALUGEL and SIGMASTAT. The specification has been amended to demarcate these terms with a registered trademark symbol, thereby rendering the objection moot.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the objection to the specification.

The specification is objected to for allegedly failing to provide antecedent basis for the phrase "polymeric 11D10 polypeptide" in claim 36. Applicants respectfully note that literal support for this phrase is provided on page 7, line 7 and on page 75, line 3 of the specification.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the objection to the specification.

Objections to the claims

Claims 5, 23, 24, 69, 70, 75, 78, 80, 86, 90, 94, and 97 are objected to for allegedly failing to limit the subject matter of a previous claim. The Examiner states that recitations of inherent properties or intended use cannot be relied upon to further limit the subject matter of the claim or claims from which a claim depends.

Applicants respectfully traverse and will further address this issue upon indication by the Office of allowable subject matter, including rewriting claims in independent form, which the Examiner has stated would remove this objection.

Claims 4, 40, 42, 60, 73, 74, 75, 76, and 84 are objected to for allegedly being substantial duplicates of claims 1, 37, 39, 59, 35, 37 and 40, 37 and 40, 43, and 35 and 73, respectively. The Examiner states that when two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim.

Applicants respectfully traverse and will address this issue upon indication by the Office of allowable subject matter. Applicants note that although claims 35 and 73 both are directed to humanized antibodies, claim 35 recites a *constant* region that is a human sequence and claim 73 recites *framework* regions that are human sequences. The framework regions are found in the variable region of an antibody.

Claims 77 and 96 are objected to as reciting a polypeptide comprising the CDRs of both the light *and* heavy chain variable regions of monoclonal antibody 11D10, whereas claim 20, upon which these claims depend recites a polypeptide comprising the CDRs of the light *or* heavy chain variable region. Claim 20 as amended is directed to a polypeptide comprising both light and heavy chain CDRs, rendering this objection moot. However, Applicants note that the term "comprises" as used in claim 20 prior to the current amendment and in new claim 98 is a term of art that permits additional unrecited elements to be included within the scope of a claim. Use of this term with respect to the present claims permits inclusion of sequences other than those which are specifically recited. MPEP § 2111.03. The term "or" does not exclude other sequences from the claim. The three CDRs of the light chain *or* the heavy chain must be comprised (*i.e.* included) within the claimed polypeptide, but other sequences may be included as well, in view of the term "comprises."

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the objection to claims 77 and 96.

Rejection under 35 U.S.C. § 101

Claims 1, 92 and 97 are rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter.

Applicants respectfully disagree with the statement in the Office Action that the subject matter of these claims cannot be distinguished from naturally occurring products because the

hybridoma that produces monoclonal antibody 11D10 was derived from a naturally-occurring lymphocyte. Office Action, page 4. Applicants respectfully submit that a hybridoma is not a naturally-occurring product, because by definition it is produced *in vitro* by fusion of a lymphocyte with an immortalized cell. The *in vitro* fusion is a manipulation that removes the lymphocyte from its natural environment and alters it so that it can grow in culture, which it cannot do in the absence of the fusion. Once altered by the fusion, the lymphocyte is no longer naturally-occurring. Although the claims as pending prior to this response do not encompass naturally-occurring products, claims 1 and 92 have been amended to recite an "isolated" antibody, solely to expedite prosecution, further distinguishing the claimed subject matter from naturally-occurring products.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 101.

Claims 20-24, 26-30, 34, 36, 39, 42, 56, 61-63, 67, and 68 are rejected under 35 U.S.C. § 101 as allegedly not supported by either a specific and substantial asserted utility, a credible asserted utility, or a well-established utility. Applicants respectfully traverse this rejection.

As discussed during the telephone interview of May 7, 2003, the specification discloses several well-established specific, substantial, and credible utilities. Any one of these uses satisfies the utility requirement. During the telephone interview, Examiner Caputa stated that Applicants' disclosure satisfies the utility requirement.

For example, the specification discloses use of polypeptides to induce an immune response, or to detect or purify an antibody that binds to 11D10. Page 86, line 16 - page 87, line 13. Use of polypeptides in such methods are well-established and routine in the art. Uses for polypeptides of the invention are described in detail on pages 86-89 of the specification. The claimed polypeptides relate to a specific, useful antibody, namely 11D10.

Applicants disagree with the Examiner's statement that use of the polypeptides of the invention to elicit an anti-HMFG immune response lacks credibility. As discussed in the recent

telephone interview, an anti-idiotype antibody *mimics* an antigen, in contrast to an idiotype antibody, which *binds* to an antigen. Therefore, it is credible that a fragment of the antibody would be capable of mimicking an antigenic epitope to which an idiotype antibody binds. Further, it is credible that a fragment of antibody 11D10 could elicit a T cell immune response since it is known in the art that very small peptide sequences can stimulate specific T cell proliferation.

In addition to elicitation of an immune response, the specification discloses other well established utilities for polypeptides of the invention, such as detection or purification of an anti-11D10 antibody. These uses are specific, since the claimed polypeptides require specifically disclosed sequences of antibody 11D10. These uses are also substantial, because these are "real world" uses that do not require further research by a person of skill in the art. A person of skill in the art would also consider these uses credible, and the Examiner has not provided any evidence to the contrary.

In order to satisfy the statutory requirement for utility, Applicants need to provide only one credible assertion of specific and substantial utility. MPEP § 2107. As discussed above, Applicants have disclosed several specific, substantial, and credible utilities that are well-established uses for polypeptides. Therefore, the presently-claimed invention satisfies the utility requirement for patentability.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 101.

Rejection under 35 U.S.C. § 112, first paragraph

Enablement rejections

Claims 20-24, 26-30, 34, 36, 39, 42, 56, 61-63, 67, and 68 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled due to lack of support by either a specific and

substantial asserted utility, a credible asserted utility, or a well established utility. Applicants respectfully traverse this rejection.

During the telephone interview of May 7, 2003, Examiner Caputa stated that the utility requirement is satisfied by Applicants' disclosure. Therefore, since the claimed invention is supported by utility, as discussed in the interview, this enablement rejection should be withdrawn.

As discussed above, the invention is supported by a number of specific, substantial, and credible utilities, such as use for detection or purification of anti-11D10 antibodies. As such, the "use" requirement of §112, first paragraph, is satisfied and this rejection may be properly withdrawn. Further, descriptions of how to make and use polypeptides of the invention for such purposes may be found in the specification, for example, on pages 77-79 and 86-89.

The Office Action states that the claimed invention is not enabled because the specification fails to provide working exemplification of use of the invention to elicit an anti-HMFG immunological response in a mammal or to induce antitumor immunity in a mammal. Office Action, page 7. "Exemplification" is not the standard for utility, but rather whether an asserted utility is specific, substantial, and credible, or well established, from the standpoint of a person of skill in the art. Therefore, it is not necessary for Applicants to exemplify use of the claimed invention to elicit an immune response in order for the invention to satisfy the enablement requirement. As discussed above, Applicants have asserted several utilities for the claimed polypeptides, including detection and purification of anti-11D10 antibodies, in addition of elicitation of an anti-HMFG immune response. As noted above, in the recent telephone interview, Examiner Caputa stated that Applicants' disclosure satisfies the utility requirement.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph. Applicants note that withdrawal of the rejection of claims 20-24, 26-30, 34, 36, 39, 42, 56, 61-63, 67, and 68 under 35 U.S.C. §101, discussed above, would render this rejection moot, and this rejection should therefore be withdrawn.

Claims 1-5, 20-24, 26-37, 39, 40, 42, 43, 54-56, 59-65, and 67-97 are rejected under 35 U.S.C. 112, first paragraph, as allegedly not enabled. Applicants respectfully traverse this rejection.

The Examiner states that the specification is not enabling for making and/or using a monoclonal antibody produced by the progeny of the hybridoma that produces monoclonal antibody 11D10, or said progeny, or a polypeptide that comprises a region of either the heavy chain or the light chain of monoclonal antibody 11D10, or a polypeptide that comprises the three complementarity-determining regions (CDRs) of either or both of the light and heavy chains of monoclonal antibody 11D10.

Solely to expedite prosecution, claims 20 and 39 have been amended to recite a polypeptide that comprises the three light chain CDRs *and* the three heavy chain CDRs. During the telephone interview of May 7, 2003, the Examiners indicated that this would be sufficient to overcome the enablement rejection of these claims.

New claims 98 and 99 recite a polypeptide comprising the three light chain CDRs *or* the three heavy chain CDRs, without the functional language relating to immunological activity of anti-idiotype antibody 11D10 and ability of the claimed polypeptide to stimulate a specific immune response against HMFG. During the telephone interview, Examiner Caputa stated that amending the claims in this way would be sufficient to abrogate the enablement rejection.

Applicants note that methods of culturing and obtaining progeny are well known in the art. Further, upon a search of the U.S. patent database, Applicants' representative found 13 issued U.S. patents that include the term "progeny" in claims which recite a hybridoma having an ATCC designation, including co-owned U.S. Patent Nos. 5,977,315, 5,977,316, 6,355,244, and 6,274,143.

For completeness, Applicants maintain that the specification provides adequate guidance to enable one of skill in the art to make and use the claimed invention without undue experimentation. For example, the specification provides methods for making 11D10 polypeptides and using these polypeptides to elicit an immune response or to detect or purify anti-11D10 antibodies.

The specification provides examples of methods for making polypeptides, for example by proteolytic or other degradation of 11D10, by recombinant methods, or by chemical synthesis (page 77, lines 13-19). Such methods are well known and routine in the art.

The specification also provides methods for using the polypeptides of the invention to elicit an anti-HMFG immunological response in a mammal, or to detect or purify anti-11D10 antibodies. Functional assays for characterization of an immunological response are provided in the specification, for example on page 84, line 4 - page 85, line 23. Such assays are routine within the art. Methods for detecting or purifying anti-11D10 antibodies are taught on page 86, line 16 - page 87, line 13. Thus, a skilled artisan would readily be able to make and use the invention based upon the disclosure in the specification.

The Examiner states that "there is evidence suggesting that the amino acid sequence set forth in this application is not the amino acid sequence of the antibody." Tripathi, et al (*Hybridoma* **18**: 193-202, 1999) teach the amino acid sequence of the light chain of monoclonal antibody 11D10. Tripathi, et al disclose Applicant's own work; yet the amino acid sequence of the antibody disclosed by Tripathi, et al differs from Applicants' disclosed amino acid sequence of the light chain of the antibody." Office Action, page 15. In response, Applicants note that the sequence differences to which the Examiner refers are in the leader sequence, not in the sequence of the mature, processed protein. Thus, these differences are not relevant to the claimed invention.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Written description

Claims 1-5, 20-24, 26-37, 39, 40, 42, 43, 54-56, 59-65, and 67-97 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not supported by adequate written description. Applicants respectfully traverse this rejection.

During the telephone interview of May 7, 2003, Examiner Caputa stated that claim 20 as amended and new claim 98 are supported by written description. With respect to claims 1-5, Applicants note that written description is provided in, *inter alia*, the form of deposit of the hybridoma.

Citing *The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement* (66 FR 1099-1111), the Examiner states that an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicants were in possession of the claimed genus. In response, Applicants note that all of the claimed polypeptides encode variable region sequences or CDR's of antibody 11D10. These sequences are relevant identifying characteristics of this genus of polynucleotides and are provided in the specification. These sequences provide common structural information about the polypeptides within the scope of the claims, showing that Applicants were in possession of the claimed genus at the time of filing. Further, as noted above, deposit of the hybridoma which produces monoclonal antibody 11D10 provides written description support for the antibody and hybridoma claims.

The Examiner further states that for inventions in an "unpredictable" art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In response, Applicants note that MPEP § 2163(3)(a)(ii) states that "[w]hat constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the *necessary common attributes or features* of the elements possessed by the members of the genus in view of the species disclosed." (emphasis added) In the instant case, Applicants have provided sequences for the variable regions, including the CDRs, which are the common features encoded by the claimed genus of polypeptides. One of skill in the art would recognize that Applicants were in possession of these features from the description in the specification. This same section of the MPEP further states that "[d]escription of a representative number of species does not require the description to be of such specificity that it

would provide individual support for each species that the genus embraces. For example, in the molecular biology arts, if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence, *but not necessarily any particular species*." (emphasis added) With respect to the present invention, Applicants have provided sufficient structural information, *e.g.*, polypeptide sequences of the variable regions of antibody 11D10, such that one of skill in the art would accept that Applicants were in possession of the full genus of polypeptides claimed. Thus, the claimed invention is supported by adequate written description.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 26 is rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants respectfully traverse this rejection.

Claim 26 is clear as written. A sequence of at least 2 contiguous amino acids of HMFG would be readily understood by one of skill in the art to mean a continuous sequence of at least 2 amino acids within the sequence of this protein, especially as further defined in view of the fact that the sequence which is referenced in the claim is within a defined, disclosed sequence, SEQ ID NO:33, as recited in the claim. A sequence of at least 2 contiguous amino acids that is identical in forward or reverse orientation to 2 contiguous amino acids of the sequence disclosed in SEQ ID NO:33 would be readily ascertainable by one of skill in the art. If the Examiner has a suggestion as to an amendment to further clarify the claim, he is invited to provide such a suggestion to Applicants.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Claim 56 is rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite due to lack of antecedent basis for the phrase "11D10 polypeptide." Solely to expedite prosecution, claim 56 has been amended to delete the term "11D10," rendering the rejection moot. However, Applicants note that lack of antecedent basis in this instance does not render this claim indefinite or in any way unclear.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 102

Claims 1-5, 37, 40, 59, 60, 69, 70, 74, 75, 88-90, 92-94, and 97 are rejected under U.S.C. 102(b) as allegedly anticipated by Bhattacharya-Chatterjee, et al. (In *Antigen and Antibody Molecular Engineering in Breast Cancer Diagnosis and Treatment,* Ceriani, RL, Ed., Plenum Press: New York, pp. 139-148, 1994). Applicants respectfully traverse this rejection.

During the telephone interview of May 7, 2003, Examiner Caputa stated that resubmission of previously-submitted declarations of co-inventors Malaya Bhattacharya-Chatterjee and Sunil Chatterjee, with correction of typographical errors which are discussed in detail below, would be sufficient to overcome this rejection. Newly-executed, corrected declarations are submitted as Exhibit A. Further, Applicants note that this reference has been withdrawn as a § 102 reference in copending application no. 08/836,455.

As discussed in the recent telephone interview and in the response filed on November 7, 2001, as well as in the preliminary amendment filed on October 8, 1998 and in the response filed on

March 26, 2001, this reference is not an appropriate § 102(b) reference because (a) it is not enabling because it does not teach and/or enable obtaining the 11D10 antibody, and does not disclose the amino acid sequence or polynucleotide coding sequence for the variable regions of 11D10, and thus cannot be used as a prior art reference; and (b) neither the 11D10 antibody nor the hybridoma producing 11D10 were made available to the public prior to filing of the application.

Applicants previously discussed in detail the mechanism of antibody formation, as well as the uniqueness of the 11D10 sequences, which were not disclosed in the cited reference, in the preliminary amendment filed on October 8, 1998. Further, neither the 11D10 antibody nor the hybridoma producing 11D10 were made accessible to the public before filing the of the priority application, as discussed in declarations by the inventors submitted on September 30, 1999.

The Examiner states that the declarations of the inventors fail to "explicitly state how the hybridoma and the antibody were controlled." Office Action, page 23. As discussed in the recent telephone interview, Applicants submit that it is not necessary for a declaration to set forth the precise means by which materials remain under the control of the declarer. In this instance, the declarations plainly state that the antibodies and hybridoma were not distributed to or provided to the public. That is the relevant question here, not the mechanism of such control. Both Malaya and Sunil Chatterjee expressly stated that they did not make the antibody or cell line available to the public. Declaration of Malaya Bhattacharya-Chatterjee, page 5; Declaration of Sunil Chatterjee, page 3. Malaya Chatterjee stated that she maintained strict and exclusive control over the distribution of the 11D10 antibody and the antibody producing cell line. Declaration of Malaya Chatterjee, page 3. Similarly, Kenneth Foon expressly stated that the use and distribution of 11D10 for clinical trials was under his strict and exclusive control. Declaration of Kenneth Foon, page 2. The inventors all signed unequivocal statements indicating that they controlled the antibodies and cell line. The means of this control is irrelevant.

The Examiner also states that the declarations do not state that neither the hybridoma nor the antibody were publicly accessible or available upon request. Office Action, page 23-24. Applicants note that both Malaya Chatterjee and Sunil Chatterjee stated that they did not make the antibody or cell line available to the public and did not believe that they were under any obligation to do so

(Declaration of Malaya Chatterjee, page 5; Declaration of Sunil Chatterjee, page 3), and Kenneth Foon stated that to the best of his knowledge and belief, the public did not obtain these materials (Declaration of Kenneth Foon, page 2).

The previously-submitted declarations of inventors Malaya Bhattacharya-Chatterjee and Sunil Chatterjee include a typographical error in a sentence declaring that to the best of their knowledge and belief, the public did not have access to the 11D10 cell line or antibody prior to filing of the application. Due to a clerical error, the word "not" was omitted and the sentence reads "the public did have access." During the telephone interview on May 7, 2003, Examiner Caputa stated that providing newly-executed declarations with these typographical errors corrected would render the declarations sufficient to overcome this rejection. New declarations, signed by Malaya Bhattacharya-Chatterjee and Sunil Chatterjee are submitted herewith as Exhibit A. Each of these declarations includes a corrected sentence in paragraph 8 that states that the public did *not* have access to the cell line or antibody prior to filing of the application.

Applicants strongly disagree with the Examiner's statement on page 25 of the Office Action that "one would not necessarily have to have access to the hybridoma producing monoclonal antibody 11D10 to make and use the claimed invention." This statement contradicts the Examiner's statement on page 23 that "it is agreed that if neither the antibody nor the hybridoma producing the antibody were accessible or available upon request to any other individual that although the cited references disclose the antibody, none of the cited references can be considered to provide an enabling disclosure of the claimed invention." As discussed above, the declarations of the inventors unequivocally state that neither the hybridoma nor the antibodies were accessible or provided to the public prior to the filing of the application. Therefore, it would not have been possible to produce the claimed polypeptides, since the sequences for the polypeptides were not available.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Claims 1, 3-5, 37, 40, 59, 60, 69, 70, 74, 75, 88-90, 92-94, and 97 are rejected under 35 U.S.C. 102(b) and/or 35 U.S.C. 102(a) as allegedly anticipated by Bhattacharya, et al. (*Cancer Immunology & Immunotherapy* **38**: 75-82, 1994) or Chakraborty, et al. (*Proceedings of the American Association for Cancer Research* **35:** 497, Abstract No. 2963, 1994). Applicants respectfully traverse this rejection.

As noted above, during the telephone interview, Examiner Caputa stated that submission of the declarations that are attached as Exhibit A would be sufficient to overcome this rejection. Further, Applicants note that these references have been withdrawn as § 102 references in copending application no. 08/836,455.

The Examiner states that these references indicate that 11D10 was known and used by others in this country before the filing date of the application and that the abstract of Chakraborty "provides evidence that the use of the antibody was disclosed publicly during a poster session at a scientific meeting." As discussed above, these references do not anticipate the claimed invention because they do not teach and/or enable obtaining the 11D10 antibody, and do not disclose the amino acid sequence or polynucleotide coding sequence for the variable regions of 11D10, and neither the 11D10 antibody nor the hybridoma producing 11D10 were made available to the public. These references are addressed in the declarations attached in Exhibit A. As noted above, during the telephone interview, Examiner Caputa stated that resubmission of these declarations with the typographical error corrected would be sufficient to overcome this rejection.

In response to the Examiner's statement regarding public disclosure of use of the antibody in a poster session, Applicants note that since neither the hybridoma nor the antibody were provided to the public prior to filing of the application, discussion of the antibody in a poster would not be sufficient to enable one of skill in the art to produce the antibody or the polypeptide sequences of the antibody.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Claims 1, 3-5, 37, 40, 59, 60, 69, 70, 74-76, 88-95, and 97 are rejected under 35 U.S.C. §102(a) as allegedly anticipated by Chakraborty, et al. (*Cancer Research* **55**: 1525-1530, 1995). Applicants respectfully traverse this rejection.

This reference has been addressed in the previously submitted declaration of Malaya Bhattacharya-Chatterjee, a corrected copy of which is submitted herewith in Exhibit A. As noted above, during the recent telephone interview, Examiner Caputa stated that submission of this corrected declaration would be sufficient to overcome this rejection. This reference represents the inventors' own work and was published less than one year prior to filing of the application. Therefore, this reference is not available as prior art under 35 U.S.C. § 102(a). Applicants note that this reference has been withdrawn as a § 102 reference in copending application no. 08/836,455.

In response to the Examiner's statement that it appears that Dr. Mukerjee made an independent inventive contribution because he was a postdoctoral fellow, as discussed in the interview, Applicants note that the declaration of Malaya Bhattacharya-Chatterjee explicitly states that Dr. Mukerjee worked under her supervision to generate and characterize 11D10 antibody, such as performing Western blots. The Examiner has provided no factual evidence to contradict Dr. Bhattacharya-Chatterjee's sworn statement that Dr. Mukerjee worked under her supervision, and has provided no factual evidence that Dr. Mukerjee made an independent contribution to the claimed subject matter. This was discussed during the telephone interview, and Examiner Caputa agreed that the Examiner had provided no factual evidence to contradict Dr. Bhattacharya-Chatterjee's statements in her declaration concerning the contributions of Dr. Mukerjee, and thus Dr. Bhattacharya-Chatterjee's declaration would serve to overcome this rejection.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(a).

Claims 1, 3-5, 37, 40, 59, 60, 69, 70, 74, 75, 88-90, 92-94, and 97 are rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Chakraborty, et al. (*Journal of Immunotherapy* **18**: 95-103, 1995).

This reference is addressed in a declaration by Malaya-Chatterjee dated September 13, 2002 and submitted on September 26, 2002 in co-pending application no. 08/836,455. A copy of this declaration is attached to this response as Exhibit B. This reference represents the inventors' own work and was published less than one year prior to filing of the application. Therefore, this reference is not available as prior art under 35 U.S.C. § 102(a). Applicants note that this reference was withdrawn as a § 102 reference in copending application no. 08/836,455.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(a).

Claims 88-90 are rejected under 35 U.S.C. 102(b) as allegedly anticipated by Kofler, et al. (*Journal of Clinical Investigation* **82:** 852-860, 1988). Applicants respectfully traverse this rejection.

Applicants do not understand this rejection. The Examiner has not pointed out which sequence or sequences disclosed in Kofler et al. he believes to anticipate the claims. Claims 88-90 recite an antibody comprising a light chain variable region amino acid sequence contained in SEQ ID NO:2 and a heavy chain variable region amino acid sequence contained in SEQ ID NO:4. An antibody such as 11D10 that includes the entire variable region sequences set forth in SEQ ID NOs: 2 and 4 are encompassed within the scope of these claims. Kofler et al. do not teach an antibody that has the entire variable region sequences set forth in SEQ ID NOs: 2 and 4. Therefore, Kofler et al. does not anticipate the claims.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

Claims 1-5, 31-33, 35, 37, 40, 43, 54, 55, 59, 60, 64, 65, and 69-97 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Bhattacharya-Chatterjee, et al. (*In Antigen and Antibody Molecular Engineering in Breast Cancer Diagnosis and Treatment,* Ceriani, RL, Ed., Plenum Press: New York, pp. 139-148, 1994) in view of Chakraborty, et al. (*Proceedings of the American Association for Cancer Research* **35:** 497, Abstract no. 2963, 1994) and in further view of Kennedy, et al. (*Biotechniques* **3:** 404-410, 1985), WO 94/11508-A2 (26 May 1994), Goldenberg (*American Journal of Medicine* **94**: 297-312, 1993), and Carter, et al. (*Proceedings of the National Academy of Sciences of the USA* **89**: 4285-4289, 1992). Applicants respectfully traverse this rejection.

During the telephone interview on May 7, 2003, Examiner Caputa stated that providing newly-executed declarations with typographical errors corrected, attached herewith as Exhibit A, would be sufficient to overcome this rejection.

A prima facie case for obviousness requires, *inter alia*, that prior art references, when combined, must teach or suggest all claim limitations. MPEP § 2143. The cited references do not teach, either singly or in combination, antibody 11D10, a hybridoma producing antibody 11D10, or a polypeptide comprising sequences of antibody 11D10 as claimed.

As discussed above, neither Bhattacharya et al. nor Chakraborty et al. is an enabling reference and further, the 11D10 antibody was not provided to the public prior to the filing date. Specifically, Bhattacharya-Chatterjee et al. and Chakraborty et al., which disclose that a hybridoma named "11D10" produces antibody 11D10 and use of antibody 11D10 to induce an anti-HMFG immune response in monkeys, respectively, do not disclose either the polypeptide sequences of 11D10, or the polynucleotide sequences that encode the polypeptides. As provided in the record, based on the nature of antibody formation, disclosure of how antibody 11D10 was generated does not provide an enabling disclosure of the amino acid sequence of 11D10, or polynucleotides

encoding 11D10. The cited references are not enabling because disclosure of the name of the 11D10 hybridoma alone would not enable one skilled in the art to deduce the polynucleotide sequence encoding the heavy or light chain variable regions of 11D10, or fragments thereof, as presently claimed. These points have been considered and accepted by the Office *twice*, in two separate cases, which resulted in issued U.S. Patent Nos. 5,977,316 and 5,935,821. Further, these two references have been withdrawn as §102(b) references in co-pending application no. 08/836,455. Withdrawal of the §102(b) rejection evidences that the Office has deemed these references to be non-enabling for the claimed sequences. As such, these references do not provide a proper basis for a § 103 rejection of these claims. Thus, neither of these references anticipates the claims. As discussed below, the combination of these two references with the other cited references does not provide the missing information and thus does not render the claimed invention obvious.

Kennedy et al. teaches that anti-idiotypic antibodies might be useful as vaccines and that chimeric versions of these antibodies may be produced. WO 94/11508 teaches anti-HMFG antibodies and polypeptides, and suggests methods for producing anti-idiotypic antibodies for HMFG. However, neither of these references teaches 11D10 antibody or the polypeptide or polynucleotide sequences encoding the light and heavy chain variable regions of 11D10 antibody.

Goldenberg discusses antibodies and derivatives thereof, including anti-idiotypic antibodies, and Carter teaches methods for producing humanized versions of monoclonal antibodies. Neither of these references teaches 11D10 antibody or the polypeptide or polynucleotide sequences encoding the light and heavy chain variable regions of 11D10 antibody.

In conclusion, the cited references do not render the instant invention unpatentable because the combination of references does not teach the specific polypeptide sequences recited in the instant claims. Further, since neither the hybridoma that produces 11D10 nor the 11D10 antibody were provided to the public prior to the filing of this application, it would not have been possible for one of skill in the art to make and use the invention.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claims 1-5, 31-33, 35, 37, 40, 43, 54, 55, 59, 60, 64, 65, and 69-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chakraborty, et al. (*Cancer Research* **55**: 1525-1530, 1995) in view of Kennedy, et al. (*Biotechniques* **3**: 404-410, 1985) and WO 94/11508-A2 (26 May 1994) and in further view of Goldenberg (*American Journal of Medicine* **94**: 297-312, 1993) and Carter, et al. (*Proceedings of the National Academy of Sciences of the USA* **89**: 4285-4289, 1992). Applicants respectfully traverse this rejection.

During the telephone interview on May 7, 2003, Examiner Caputa stated that providing newly-executed declarations with typographical errors corrected, attached herewith as Exhibit A, would be sufficient to overcome this rejection.

To support a rejection under 35 U.S.C. §103(a), a reference must be available as prior art under §102 (MPEP § 2141.01). As discussed above, Chakraborty et al. is not available as prior art under § 102(a) because it represents work that was done under the direction of the inventors and was published less than one year prior to the filing of the present application. Applicants note that this reference was cited and withdrawn as a § 102 reference in related application U.S. serial no. 08/836,455, which has the same priority date as the instant application. The roles and contributions of the authors of the Chakraborty et al. reference have been addressed in the Declaration of Malaya Bhattacharya-Chatterjee, a corrected version of which is resubmitted herewith in Exhibit A. This declaration shows that the Chakraborty et al. reference is not available as a § 102(a) or § 102(f) reference, and since it was published less than one year prior to the filing date, it is also not available as a § 102(b) reference. Therefore, Chakraborty et al. is not available as a supporting reference for a § 103(a) rejection since it is not a prior art reference under §102.

The Examiner states that the publication policy of *Cancer Research* rendered "the [11D10] antibody and the hybridoma . . . attainable, upon request, by any academic researcher, provided that the authors were willing and able to comply with the acknowledged and accepted policy of the journal." Office Action, page 33. The Examiner further states that "[t]he fact that Applicants did not distribute the antibody or the hybridoma to any other person does not constitute evidence that the

antibody and the hybridoma were not accessible or attainable upon request by another." Office Action, page 34. As discussed above, the *Cancer Research* paper has been previously addressed in the declaration by Malaya Bhattacharya-Chatterjee, resubmitted in Exhibit A, which explained that it represented the inventors' own work, which was performed under their supervision and control. Since it was published less than a year prior to filing of the application, this reference does not constitute prior art under 35 U.S.C. §102(a).

In view of the unavailability of this reference under § 102(a), the publication policy of *Cancer Research* is moot. However, for completeness, Applicants reiterate their previous position with respect to this policy. As discussed above, Applicants have expressly stated in previously-filed declarations that 11D10-producing hybridoma and 11D10 antibody remained under their control and had not been released to the public prior to the filing date of the present application. Even if the publication policy of *Cancer Research* were effective to render the antibody or hybridoma attainable upon request, which Applicants do not agree with or concede, the fact remains that the inventors never provided them to others. Applicants reiterate the point that *Cancer Research* merely has a *policy* that authors agree to make research materials available to others, but does not *require* authors to do so. In her declaration, Malaya Chatterjee expressly stated, "I did not make the antibody or cell line available to the public, and *I did not believe I was under any obligation to make the antibody or cell line available*" (p. 5, Declaration of Malaya Bhattacharya-Chatterjee, emphasis added). Despite the policy of *Cancer Research*, Dr. Chatterjee did not believe that she was obligation to provide these materials to others, and indeed did not do so. Further, even if, for the sake of argument, the publication policy of *Cancer Research* rendered the 11D10 antibody or hybridoma attainable by others, this did not occur before the invention by the Applicant. As discussed in the declaration by Malaya Bhattacharya-Chatterjee, the work published in the *Cancer Research* article was performed in her laboratory with the co-authors of the paper working under her direct supervision. Therefore, this publication did not appear before the invention by the Applicants, and since the publication policy of *Cancer Research* went into effect concurrent with publication, this policy likewise did not come into effect before the invention by the Applicants, removing it from the purview of §102(a). Logically, an antibody (or the hybridoma producing the antibody) could not become available until after it was produced.

A prima facie case for obviousness requires, *inter alia*, that prior art references, when combined, must teach or suggest all claim limitations (MPEP § 2143). The cited references do not teach, either singly or in combination, an isolated polynucleotide that encodes a polypeptide comprising the three light chain or heavy chain CDRs of antibody 11D10, as recited in the present claims. Even if Chakraborty et al. were available as a prior art reference, Applicants reiterate their previous argument that this reference does not provide an enabling disclosure with respect to the instant claims, because disclosure of the 11D10 hybridoma alone would not enable one of skill in the art to deduce the claimed polynucleotide sequences. The other cited references do not supply this missing element.

Kennedy et al. teaches that anti-idiotypic antibodies might be useful as vaccines and that chimeric versions of these antibodies may be produced. WO 94/11508 teaches anti-HMFG antibodies and polypeptides, and suggests methods for producing anti-idiotypic antibodies for HMFG. However, neither of these references teaches 11D10 antibody or the polynucleotide sequences encoding the light and heavy chain variable regions of 11D10 antibody.

Goldenberg discusses antibodies and derivatives thereof, including anti-idiotypic antibodies, and Carter teaches methods for producing humanized versions of monoclonal antibodies. Neither of these references teaches 11D10 antibody or the polypeptide or polynucleotide sequences encoding the light and heavy chain variable regions of 11D10 antibody.

In conclusion, the cited references do not render the instant invention unpatentable because the combination of references does not teach the specific polypeptide sequences recited in the instant claims. Further, as discussed above, since neither the hybridoma that produces 11D10 nor the 11D10 antibody were provided to the public prior to the filing of this application, it would not have been possible for one of skill in the art to deduce these sequences.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Double Patenting

Claims 1-5, 37, 40, 43, 54, 55, 59, 60, 69, 70, 74-76, and 88-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 37, 40, 43, 54, and 55 of copending application no. 08/836,455. As discussed during the recent interview, the claims of copending application no. 08/836,455 that are referred to in this rejection were subject to a restriction requirement and were withdrawn as drawn to a non-elected invention. These claims will be canceled in 08/836,455 upon obtaining allowable subject matter. A copy of the restriction requirement is attached here as Exhibit C.

Applicants also bring co-owned U.S. Patent No. 6,274,143 and co-owned, copending application no. 10/367,506 to the Examiner's attention. U.S. Patent No. 6,274,143 is the subject of an obviousness-type double patenting rejection in copending application no. 08/836,455.

CONCLUSION

Applicants have, by way of the amendments and remarks presented herein, removed the issues for the rejections and addressed all issues that were raised in the outstanding Office Action. Accordingly, reconsideration and allowance of the pending claims are respectfully requested. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 304142000321.

Respectfully submitted,

Dated: August 11, 2003 By: Jill A. Jacobson

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